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EXAMINER	
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1632	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/802,228	PULST, STEFAN	
	Examiner	Art Unit	
	Paul Dowell	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 November 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-31* is/are pending in the application.

4a) Of the above claim(s) *9,10 and 13-15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,11,12 and 16-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *3/16/2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election of claims 1-8, 11, 12, 16-31 (group I) in the reply filed on 11/30/2005 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). The restriction requirement is still deemed proper and is therefore made FINAL.

Claims 9, 10, 13-15 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 11/30/2005.

Claims 1-8, 11, 12, 16-31 are under examination.

Specification

The abstract of the disclosure is objected to because the term "SCA-2" is not defined (i.e. spinocerebellar ataxia 2) at the first recitation of said term. Correction is required. See MPEP § 608.01(b).

Claim Objections

Claim 1 is objected to because the term "SCA-2" is not defined (i.e. spinocerebellar ataxia 2) at the first recitation of said term. Appropriate correction is required.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Applicant is advised that should claim 1 be found allowable, claim 16 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). Claim 1 is drawn to a vector suitable for use in a human comprising a polynucleotide, wherein said polynucleotide encodes a SCA-2 (Spinocerebellar Ataxia 2) polypeptide and claim 16 is drawn to a vector for the delivery of a SCA-2 therapeutic element to a human for the treatment of obesity wherein the

vector comprises an expression cassette encoding the SCA-2 therapeutic. Claim 16 is a substantial duplicate of claim 1.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-8, 16-19 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 34 and 35 of **U.S. Patent No. 6,515,197 B1** ('197). Although the conflicting claims are not identical, they are not patentably distinct from each other.

In the instant application, claims 1-6 are drawn to a vector comprising a nucleic acid encoding SCA-2 protein, claims 7 and 8 are drawn to a pharmaceutical composition comprising a biologically effect amount of a nucleic acid encoding SCA-2 protein and claims 16-19 are drawn to a vector for the delivery of a SCA-2 therapeutic element comprising an expression cassette encoding the SCA-2 therapeutic. Claim 34

of '197 is drawn to a DNA construct comprising a DNA sequence encoding a human ataxin-2 polypeptide having a polyglutamine tract comprising about 58 glutamines, operationally linked to a Purkinje cell-specific expression element and claim 35 of '197 is drawn to a vector comprising the DNA construct of claim 34. Ataxin-2 and SCA-2 are synonymous terms and the recitation of claim 34 of '197, "a human ataxin-2 polypeptide having a polyglutamine tract comprising about 58 glutamines", would encompass a human ataxin-2/SCA-2 polypeptide having a polyglutamine tract comprising 22 glutamines, the wild type human ataxin-2/SCA-2 consisting of 22 glutamines as shown in SEQ ID NO:1 (SEQ ID NO:1 encoding SEQ ID NO:2) of the instant application. Thus, Claims 34 and 35 of '197 are entirely encompassed by claims 1-8, 16-19 of the instant application.

Claims 1-8, 16-19 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 4 and 7 of **U.S. Patent No. 6,844,431 B1** ('431). Although the conflicting claims are not identical, they are not patentably distinct from each other.

In the instant application, claims 1-6 are drawn to a vector comprising a nucleic acid encoding SCA-2 protein, claims 7 and 8 are drawn to a pharmaceutical composition comprising a biologically effect amount of a nucleic acid encoding SCA-2 protein and claims 16-19 are drawn to a vector for the delivery of a SCA-2 therapeutic element comprising an expression cassette encoding the SCA-2 therapeutic. Claim 4 of '431 is drawn to an isolated nucleic acid encoding the amino acid sequence as set forth

at SEQ ID NO:3, with SEQ ID NO:3 being the amino acid sequence of the human SCA-2 protein. Claim 7 of '431 is drawn to a vector comprising DNA according to claim 4. The vector of claim 7 of '431 is generic to the vectors of claims 1-8, 16-19 of the instant application and as such claims 1-8, 16-19 of the instant application are entirely encompassed by claims 7 and 8 of '431.

Claims 1, 7, 16-19 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 13-15 of **copending Application No. 10/141,541** ('541). Although the conflicting claims are not identical, they are not patentably distinct from each other.

Claim 1 of the instant application is drawn to a vector comprising a polynucleotide, wherein said polynucleotide encodes a SCA-2 polypeptide. Claim 7 is drawn to a pharmaceutical composition comprising a biologically effective amount of a polynucleotide encoding a SCA-2 polypeptide. Claims 16-19 are drawn to a vector comprising an expression cassette encoding a SCA-2 therapeutic (claim 16), wherein the SCA-2 therapeutic is selected from the group consisting of a SCA-2 polypeptide, a SCA-2 protein and a SCA-2 protein fragment (claim 17), wherein the expression cassette comprises a plurality of functional elements (e.g. host cell origin of replication, suitable promoter, heterologous genetic element; claim 18), wherein the vector is a viral vector (e.g. retrovirus, adenovirus; claim 19). Claims 13 and 14 of '541 are drawn to a DNA construct comprising exon 1 of a SCA-2 gene having an inserted selectable marker sequence (claim 13), wherein said selectable marker sequence comprises a

neomycin resistance gene (claim 14) and claim 15 of '541 is drawn to a vector comprising the DNA construct of claim 13. The nucleic acid encoding the SCA-2 polypeptide of claims 1, 7, 16-19 of the instant application is generic to the nucleic acid comprising exon 1 of a SCA-2 gene of claims 13-15 of '541; and the vector of claim 15 of '541 is generic to the vectors of claims 1, 7, 16-19 of the instant application. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-8, 16-19 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 2 and 7 of **copending Application No. 10/750,323** ('323). Although the conflicting claims are not identical, they are not patentably distinct from each other.

Claims 1-6 of the instant application are drawn to a vector comprising a nucleic acid encoding SCA-2 protein, claims 7 and 8 are drawn to a pharmaceutical composition comprising a biologically effect amount of a nucleic acid encoding SCA-2 protein and claims 16-19 are drawn to a vector for the delivery of a SCA-2 therapeutic element comprising an expression cassette encoding the SCA-2 therapeutic. Claim 1 of '323 is drawn to an isolated nucleic acid encoding a mammalian SCA-2 polypeptide, claim 2 of '323 is drawn to the isolated nucleic acid of claim 1 which is DNA and claim 7 of '323 is drawn to a vector comprising the isolated nucleic acid of claim 2. The vector comprising the nucleic acid encoding a mammalian SCA-2 polypeptide of claims 1, 2 and 7 of '323 is generic to the vectors of claims 1-8 and 16-19 of the instant application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-8, 11, 12, 17-24 and 26 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claims 1, 7, 11, 17 and 26 recite "SCA-2 polynucleotide" and reasonably interpreted read on genes encoding SCA-2 polynucleotides. Genes are considered products of nature and as such are considered non-statutory subject matter. Claims 2-6 depend from claim 1, claim 8 depends from claim 7, claim 12 depends from claim 11, claims 18 and 19 depend from claim 17, and claims 20-24 depend from claim 19 and therefore are likewise rejected. Amending the instant claims to recite --isolated SCA-2 polynucleotide-- may overcome the instant rejection.

Claim 24 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claim 24 recites, "The cell of claim 21, wherein the cell comprises a neural cell". Claim 20, from which claim 21 depends, appears to be drawn to a method for introducing a SCA-2 therapeutic into human cells. Claim 24 does not recite an isolated cell and reasonably interpreted reads on a cell within a human. Humans are considered non-statutory subject matter.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 11, 12, 20-31 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

While determining whether a specification is enabling, one considers whether the claimed invention provides sufficient guidance to make and use the claimed invention, if not, whether an artisan would have required undue experimentation to make and use the claimed invention and whether working examples have been provided. When determining whether a specification meets the enablement requirements, some of the factors that need to be analyzed are: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill, the level of predictability in the art, the amount of direction provided by the inventor, the existence of working examples, and whether the quantity of any necessary experimentation to make or use the invention based on the content of the disclosure is "undue" (In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)).

Furthermore, the USPTO does not have laboratory facilities to test if an invention will function as claimed when working examples are not disclosed in the specification,

therefore, enablement issues are raised and discussed based on the state of knowledge pertinent to an art at the time of the invention, therefore skepticism raised in the enablement rejections are those raised in the art by artisans of expertise.

The instant claims are drawn to methods of treating obesity in humans comprising administering vectors, wherein said vectors comprise a nucleic acid encoding SCA-2 protein. The specification discloses the SCA-2 protein product and its domains (Figure 1), the increase in body weight gain observed in SCA-2 knockout mice compared to wild-type mice (Figure 2), body weight and food intake comparisons between SCA-2 knockout mice, SCA-2 hemizygotes and wild type mice (Figures 3-6) and greater weight gain in SCA-2 knockout and SCA-2 hemizygous mice when compared to wild type mice regardless of food availability (Figure 7). The specification concludes, based on the results disclosed in Figures 2-7, that the SCA-2 gene has been identified as a regulator of normal body weight and the absence of the SCA-2 gene leads to obesity (page 4, paragr. 0017). The specification discloses that the SCA-2 therapeutics (e.g. nucleic acid encoding SCA-2 protein or SCA-2 proteins or fragments thereof) of the present invention may be used for the reversal or prevention of stress-induced obesity in predisposed individuals and that the compositions and methods of the present invention may be useful in the prevention or reversal of obesity brought about by a high-fat diet (page 22, paragr. 0070). The specification discloses a laundry list of routes through which said SCA-2 therapeutics can be administered including orally, rectally, vaginally, topically, intratracheobronchially and via injection (subcutaneous, intramuscular or intravenous; page 30, paragr. 0089 to page 31, paragr.

0090). The specification discloses that "typically the dosage will be 0.001 to 100 milligrams of SCA-2 therapeutic per kilogram subject body weight" and "doses in the range of 0.01 to 1 mg per kilogram of patient body weight may be utilized for a therapeutic composition that is administered" (page 33, paragr. 0096). The specification discloses two prophetic working examples: Example I describes SCA-2 protein administered parenterally for 28 consecutive days to SCA-2 knockout mice, SCA-2 hemizygous mice and wild type mice after which weight gain and food intake will be measured (page 34, paragr. 0099). Example II describes administration of nucleic acid encoding SCA-2 protein to the same groups of mice. In Example II, an unspecified viral vector comprising the nucleic acid encoding SCA-2 protein is injected intravascularly at doses ranging from 10^8 to 10^{10} pfu per gram weight, after which food consumption, body weight and plasma levels of glucose and insulin are measured (page 34, paragr. 00100 to page 35).

Claim 11 is drawn to a method of treating obesity comprising the administration of a pharmaceutical composition comprising a biologically effective amount of a SCA-2 polynucleotide and an acceptable carrier. Claim 20 is drawn to a method for introducing a SCA-2 therapeutic into a human for the treatment of obesity comprising transducing a cell with the viral vector of claim 19. Claim 25 is drawn to a method for introducing a SCA-2 therapeutic into a human for the treatment of obesity comprising transfecting a cell with a plasmid comprising an expression cassette encoding the SCA-2 therapeutic. Claims 12, 21-24, 26-31 depend from one of claims 11, 20 or 25.

The breadth of independent claims 11, 20 and 25 is such that the claimed methods read on administration (claim 11), transduction (claim 20) or transfection (claim 25) of vectors comprising a nucleic acid encoding SCA-2 protein to any organism, even an organism distinct from the organism being treated. For example, claim 11 recites a step of administration of a pharmaceutical composition but does not recite an active step specifying to what is administered. Further, the breadth of claims 20 and 25 is such that the claimed methods read on transduction or transfection of any cells, even cells not contained within the organism to be treated (e.g. any cells would encompass bacterial cells). Dependent claims 23 and 30 further limit the cell types to be transduced or transfected by the claimed methods but the breadth of claims 23 and 30 is such that the claims read on any cells, even cells not contained within the organism and as such would encompass those cell types from a pig or a bird, for example. Still further, the breadth of claims 11, 20 and 25 is such that the claimed methods read on administration, transduction or transfection of any SCA-2 polynucleotide including those nucleic acids encoding mouse SCA-2 protein (which does not contain a polyQ repeat), human SCA-2 protein (which contains a 21 amino acid polyQ repeat) or any fragment or derivation thereof. The specification discloses a schematic illustration of the domains of the SCA-2 protein but provides no specific guidance as to which nucleic acids encoding which SCA-2 proteins would be operative in the claimed methods of treating obesity. The specification discloses no working examples demonstrating that administration of any nucleic acid encoding any SCA-2 proteins or fragments thereof have any effect on weight gain in any organism. Thus, an artisan would experience undue experimentation

because neither the specification nor the art of record at the time of the invention provide specific guidance as to how an artisan would practice the claimed methods as such with a reasonable expectation of success.

The specification provides no evidence or specific guidance to allow an artisan to practice the claimed method of administering, transducing or transfecting any SCA-2 therapeutic (i.e. nucleic acid encoding SCA-2 protein delivered as a plasmid or viral vector or SCA-2 protein delivered directly) to any organism, particularly humans, for the treatment of any type of obesity (i.e. stress-induced obesity as recited by claim 12 or any other type of obesity) with a reasonable expectation of success. The specification discloses only that mice containing a deletion of the gene encoding SCA-2 protein exhibit increased weight. The specification discloses no evidence, direct or indirect, that administering, transducing or transfecting any SCA-2 therapeutic to or into the cells of an organism, either *ex vivo* or *in vivo*, will result in prevention or treatment of obesity. The specification discloses evidence of a correlation between disruption of the gene encoding the SCA-2 protein and increased weight in a single strain of mice, although it is noted that the specification does not disclose the strain of mouse of the disclosed SCA-2 KO mouse. Such evidence is not enabling for the claimed methods because observation of a phenotype, particularly a weight gain or metabolic phenotype, in a single strain of mice where the gene encoding SCA-2 protein has been knocked out does not provide enabling support for a method of reversing or treating said phenotype by administering additional genetic material related to said gene or by administering a protein encoded by said gene in a wild type genetic background.

The art of record at the time of the invention recognized the unpredictability of genetic backgrounds on obesity and metabolic phenotypes in mice. For example, when discussing the obese phenotype of transgenic mice in which orexin-containing neurons were ablated by orexigenic-specific expression of a truncated ataxin-3 gene product, Hara et al **(Neuron, 30: 345-354, 2001)** teach that: "The observed metabolic differences between orexin-ataxin-3 mice and *pre-pro-orexin* knockout mice may stem from different genetic backgrounds and environmental effects. Indeed, metabolic phenotypes are known to be very sensitive to genetic background and environmental factors" (page 352, col. 2, paragr. 3, lines 6-11). Thus, how would an artisan know that the disclosed single strain of SCA-2 knockout mice was even a predictive animal model of obesity? In addition to the unpredictable effects of genetic background and environmental factors on the manifestation of obesity, the art of record at the time of the invention is silent with respect to any functional role for SCA-2 in regulating obesity. Further, the art of record at the time of the invention recognized the differences between mouse and human genes encoding SCA-2 protein. For example, Huynh et al **(Nature Genetics, 26: 44-50, 2000)** teaches that the human SCA-2 protein (termed ataxin-2 by Huynh) contains a 21 amino-acid polyQ repeat that, upon expansion into larger polyQ repeats, is thought to play a role in certain neurodegenerative diseases. In contrast, the mouse SCA-2 protein has only one glutamine at the site of the human polyQ repeat (see entire document and in particular page 44, col. 1, paragr. 1 to col. 2, paragr. 3). Thus, how would an artisan know that the disclosed single strain of SCA-2 knockout mice was even related to human obesity considering the known differences between human and mouse SCA-2

proteins? Still further, Claims 23 and 30 further limit the claimed method to targeting SCA-2 therapeutics to adipocytes, muscle cells and/or neural cells. Huynh teaches that SCA-2 protein "had a cytoplasmic location in normal brain and was expressed in Purkinje cells and specific groups of brainstem and cortical neurons" (page 44, paragr. 2, lines 12-15). Nechiporuk et al **(Human Molecular Genetics, 7:1301-1309, 1998)** teaches that SCA-2 mRNA is expressed in mouse skeletal muscle (page 1302, col. 2, paragr. 2, lines 1-3, page 1304, Figure 3A). The art of record at the time of the invention is silent with respect to expression of SCA-2 in adipocytes and is silent with respect to the function of SCA-2 in adipocytes or muscle tissue. The breadth of claim 30 is such that is reads on targeting any neural cells, not just neural cells that are Purkinje cells, cells of specific groups of brainstem or cortical neurons. Thus, how would an artisan know with any predictable degree of success, that targeting adipocytes, muscle cells and/or neural cells, with a SCA-2 therapeutic would reduce or treat obesity in a human subject? Expression of SCA-2 in any intended target tissue or target cell, or the known role of a particular target tissue or cell in a particular disease (e.g. the known role of adipocytes in obesity) alone does not provide enabling support for a method of treating a particular disease by targeting expression of SCA-2 to any one particular tissue or cell type.

Even with an enabling disclosure as to the potential efficacy of treating obesity in humans by administering SCA-2 therapeutics, the art of gene therapy is unpredictable and numerous factors complicate the gene delivery art which would not have been shown to be overcome by routine experimentation. These include, for example, the fate

of a viral vector itself (volume of distribution, rate of clearance into the tissues, etc.), the fraction of vector taken up by the target cell population, the rate of degradation of the DNA, the level of mRNA produced, the stability of the mRNA produced, the amount and stability of the protein produced, and the protein's compartmentalization within the cell, or its secretory fate, once produced. While progress has been made in recent years for *ex vivo* and *in vivo* gene transfer, targeting *ex vivo* genetically modified cells or *in vivo* vector targeting to desired tissues and organs continues to be unpredictable and inefficient. Gardlik et al **(Medical Science Monitor, 11:RA110-121, 2005)** reporting on the recent developments of gene therapy recognize the continuing unpredictable and troublesome nature of gene therapy in general (see entire document and in particular page RA119):

> Although clinical trials have already started, there are still numerous limitations that must be solved before routine clinical use. Nevertheless, it can be expected that future research will bring tissue- and disease-specific delivery strategies and that this hurdle will be overcome at last.

In the instant case, the specification fails to teach one of skill in the art how to overcome the unpredictability for vector targeting such that efficient gene transfer is achieved.

In summary, the specification primarily fails to establish a clear nexus between over-expression of SCA-2, through administration of either nucleic acid encoding SCA-2 or direct administration of SCA-2 protein, and reduction or treatment of obesity in any organism. Neither the specification as filed nor the art of record at the time of the invention provide sufficient guidance to practice the claimed invention and an artisan of skill would have required extensive experimentation. Such experimentation will be

undue because of the unpredictability of the role of SCA-2 in regulating obesity, the unpredictability of treating obesity by administering a SCA-2 therapeutic comprised of a nucleic acid encoding any SCA-2 protein or variant thereof from any species, the unpredictability of obesity and the influences of genetic background and environment, and the unpredictability of *ex vivo* or *in vivo* gene therapy in general. The specification does not provide sufficient guidance to address these issues for an artisan to practice the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2, 11, 20-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 11 is incomplete. Claim 11 is drawn to a method for treating obesity comprising the administration of a pharmaceutical composition comprising a biologically effective amount of a nucleic acid encoding SCA-2 protein and an acceptable carrier; however, the instant claim does not recite any positive steps which clearly relate back to the preamble. Therefore, it is unclear how the step of administration of said pharmaceutical composition relates to the method for treating obesity and whether the goal of said method has been resolved.

Claim 20 is incomplete. Claim 20 is drawn to a method for introducing a SCA-2 therapeutic into a human for the treatment of obesity comprising transducing the cell

with the vector of claim 19; however, the instant claim does not recite any positive steps which clearly relate back to the preamble. Therefore, it is unclear how the step of transducing the cell with the vector of claim 19 relates to the method for introducing a SCA-2 therapeutic into a human for the treatment of obesity and whether the goal of said method has been resolved.

Claim 25 is incomplete. Claim 25 is drawn to a method for introducing a SCA-2 therapeutic into a human for the treatment of obesity comprising transfecting a cell with a plasmid comprising an expression cassette encoding the SCA-2 therapeutic; however, the instant claim does not recite any positive steps which clearly relate back to the preamble. Therefore, it is unclear how the step of transfecting a cell with a plasmid comprising an expression cassette encoding the SCA-2 therapeutic relates to the method for introducing a SCA-2 therapeutic into a human for the treatment of obesity and whether the goal of said method has been resolved.

There is insufficient antecedent basis for the limitations in the following claims:

Claim 2 depends from claim 1 and recites the limitation "wherein said polynucleotide sequence"; claim 1 recites “a polynucleotide”, not a polynucleotide sequence.

Claim 20 depends from claim 19 and recites the limitation “the cell”; claim 19 does not recite a cell.

Claims 21 and 22 depend from claim 20 and recite “wherein the transduction”; claim 20 recites “transducing”, not the transduction.

Claim Rejections - 35 USC § 102

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-8, 16-19 are rejected under 35 U.S.C. 102(b) as being anticipated by Pulst et al **(U.S. Patent 6,515,197 B1 issued 2/4/2003)**.

Claims 1-6 are drawn to a vector comprising a nucleic acid encoding SCA-2 protein, claims 7 and 8 are drawn to a pharmaceutical composition comprising a biologically effect amount of a nucleic acid encoding SCA-2 protein and claims 16-19 are drawn to a vector for the delivery of a SCA-2 therapeutic element comprising an expression cassette encoding the SCA-2 therapeutic.

Pulst teaches various vectors (e.g. DNA and retroviral vectors) comprising a nucleic acid encoding SCA-2 polypeptides including nucleic acid encoding SCA-2 of human origin (col. 8, lines 36-54 and col. 11, lines 11-32). Further, Pulst teaches various vector elements (e.g. promoters, enhancers, selectable markers) to be used with nucleic acid encoding SCA-2 polypeptides (col. 13, lines 7-15 and col. 13, line 66 to col. 14, line 17). Thus, Pulst anticipates the instant claims.

It is noted to Applicant that:

> When the structure recited in the reference is substantially identical to that of the claims, claimed properties or functions are presumed to be inherent. See MPEP 2112.01 and *In re Best,* 195 USPQ 430, 433 (CCPA 1997). The office does not have the facilities for examining and comparing applicant's product with the product of the prior art in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is upon the applicant to prove that the claimed products are functionally different than those taught by the prior art and to establish patentable differences. See *Ex parte Phillips*, 28 USPQ 1302, 1303 (BPAI 1993), *In re Best*, 562 F.2d

1252, 195 USPQ 430 (CCPA 1977) and *Ex parte Gray*, 10 USPQ2d 1922, 1923 (BPAI 1989).

Claims 1-8, 16-19 are rejected under 35 U.S.C. 102(b) as being anticipated by Pulst et al **(WO 97/42314, 11/13/1997)**.

Pulst teaches a vector comprising an isolated nucleic acid encoding a mammalian SCA-2 polypeptide (page 74, claims 1, 2 and 7). Said vector taught by Pulst is generic to the vectors of claims 1-8, 16-19 of the instant application and thus Pulst anticipates the instant claims.

It is reiterated to Applicant that:

> When the structure recited in the reference is substantially identical to that of the claims, claimed properties or functions are presumed to be inherent. See MPEP 2112.01 and *In re Best,* 195 USPQ 430, 433 (CCPA 1997). The office does not have the facilities for examining and comparing applicant's product with the product of the prior art in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is upon the applicant to prove that the claimed products are functionally different than those taught by the prior art and to establish patentable differences. See *Ex parte Phillips*, 28 USPQ 1302, 1303 (BPAI 1993), *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte Gray*, 10 USPQ2d 1922, 1923 (BPAI 1989).

Conclusions

No claims are allowed.

If Applicants should amend the claims, a complete and responsive reply will clearly identify where support can be found in the disclosure for each amendment. Applicants should point to the page and line numbers of the application corresponding

to each amendment and provide any statements that might help to identify support for the claimed invention (e.g. if the amendment is not supported *in ipsis verbis*, clarification on the record may be helpful). Should Applicants present new claims, Applicants should clearly identify where support can be found in the disclosure.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Paul Dowell whose telephone number is 571-272-5540. The examiner can normally be reached on M-F, 8-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram R. Shukla, can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Paul Dowell
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PRIMARY EXAMINER